

THAT WHICH IS CLAIMED IS:

1. A method for detecting a pathological condition *in vivo*, comprising:  
administering a bolus of hyperpolarized  $^{129}\text{Xe}$  to a patient;  
delivering a volume of said hyperpolarized  $^{129}\text{Xe}$  to at least one region of  
interest in the body of the patient *in vivo*;  
5       applying a resonant RF pulse sequence to said hyperpolarized  $^{129}\text{Xe}$  in the  
region of interest;  
      detecting a response signal of said hyperpolarized  $^{129}\text{Xe}$  to said pulse sequence  
via magnetic resonance spectroscopy, wherein said response signal is a spectrum of  
data having a plurality of spectral peaks;  
10       identifying at least one spectral peak of interest in said response signal;  
      analyzing said at least one identified spectral peak of interest;  
      comparing said at least one identified peak to a corresponding at least one  
spectral peak in a standard spectrum, wherein the standard spectrum is a  
predetermined magnetic resonance spectroscopic spectrum of hyperpolarized  $^{129}\text{Xe}$   
15       which includes spectra related to a desired pathological condition under analysis; and  
      determining the presence of at least one pathological condition based on said  
comparing step.
2. A method for detecting a pathological condition according to Claim 1,  
20       wherein said analyzing step includes quantifying the size of said peak by at least one  
of calculating the area under said spectral peak of interest or calculating the amplitude  
of the spectral peak of interest.
3. A method for detecting a pathological condition according to Claim 2,  
25       further comprising:  
      measuring the extent of polarization of said hyperpolarized  $^{129}\text{Xe}$  proximate in  
time and prior to said administering step;  
      measuring the volume of hyperpolarized  $^{129}\text{Xe}$  administered to the patient,  
wherein; and

normalizing the quantified value of the spectral peak of interest by adjusting the value based on the measured extent of polarization of and volume of hyperpolarized  $^{129}\text{Xe}$  determined in said measuring steps.

5           4.       A method for detecting a pathological condition according to Claim 1, wherein said analyzing step quantifies the amplitude or area under the curve of said spectral peak of interest, said method further comprising normalizing said spectral peak of interest by dividing the quantified value of said at least one spectral peak of interest by the corresponding value of another spectral peak within the response signal  
10       spectrum.

          5.       A method for detecting a pathological condition according to Claim 4, wherein the quantified value of said at least one spectral peak of interest is divided by the quantified value of the spectral peak representing the dissolved phase  $^{129}\text{Xe}$  in  
15       plasma.

          6.       A method for detecting a pathological condition according to Claim 4, wherein the quantified value of said at least one spectral peak of interest is divided by the quantified value of the spectral peak representing the dissolved phase  $^{129}\text{Xe}$  in red  
20       blood cells.

          7.       A method for detecting a pathological condition according to Claim 1, wherein said pathological condition is a degenerative disease, and said method further comprises identifying the extent of progression of said determined pathological  
25       condition.

          8.       A method for detecting a pathological condition according to Claim 7, wherein said standard spectrum is a spectrum obtained from the patient undergoing analysis prior to and temporally spaced apart in time from when said response  
30       spectrum of said detecting step is obtained.

9. A method for detecting a pathological condition according to Claim 8, wherein said comparing step is used to monitor the progression of said pathological condition.

5 10. A method for detecting a pathological condition according to Claim 8, wherein said comparing step is used to monitor the efficacy of a therapeutic treatment regimen.

10 11. A method for detecting a pathological condition according to Claim 7, wherein said standard spectrum corresponds to a spectrum representative of subjects in a corresponding population segment identified as being free of said at least one pathological condition.

15 12. A method for detecting a pathological condition according to Claim 1, wherein said at least one region of interest comprises the coronary arteries.

20 13. A method for detecting a pathological condition according to Claim 12, wherein said determining step assesses the likelihood of the presence or absence of coronary artery disease.

14. A method for detecting a pathological condition according to Claim 1, wherein said at least one region of interest comprises the brain.

25 15. A method for detecting a pathological condition according to Claim 1, further comprising:

acquiring a background spectrum of hyperpolarized  $^{129}\text{Xe}$  in the blood of the patient; and

subtracting said background spectrum from said response signal spectrum.

30 16. A method for detecting a pathological condition according to Claim 1, wherein said resonant RF pulse sequence is selected to filter out  $^{129}\text{Xe}$  signal data

associated with the interaction of the  $^{129}\text{Xe}$  with non-targeted cells in the region of interest.

17. A method for detecting a pathological condition according to Claim 5 16, wherein said RF pulse sequence is selected such that it filters out signals from  $^{129}\text{Xe}$  in flowing blood.

18. A method for detecting a pathological condition according to Claim 10 16, wherein said RF pulse sequence is selected such that it filters out undesirable signals based on at least one contrast parameter.

19. A method for detecting a pathological condition according to Claim 15 18, wherein said at least one contrast parameter is chosen from the group consisting of  $D$ ,  $T_1$ ,  $T_{1\rho}$ ,  $T_2$ , and  $T_2^*$ .

20. A method for detecting a pathological condition according to Claim 19, wherein said RF pulse sequence is a  $T_2$ -weighted pulse sequence selected to filter out hyperpolarized  $^{129}\text{Xe}$  signal associated with the blood cells and plasma in the region of interest.

21. A method for detecting a pathological condition according to Claim 20 19, wherein said RF pulse sequence is a  $T_1$  based pulse sequence selected to filter out hyperpolarized  $^{129}\text{Xe}$  signal associated with the blood cells and plasma in the region of interest by delaying the signal acquisition a predetermined time after administration 25 of the hyperpolarized gas to the patient, the predetermined time being about 10 seconds to 1 minute after cessation of the *in vivo* administration.

22. A method for detecting a pathological condition according to Claim 1, 30 wherein said administering step is carried out by breath-hold delivery, during which the patient inhales a quantity of hyperpolarized  $^{129}\text{Xe}$ , holds his or her breath, and then, after a suitable time, exhales to resume normal breathing, and wherein said RF

pulse sequence is initiated during or after said patient exhales to thereby suppress a response from non-targeted regions.

23. A method for detecting a pathological condition according to Claim 1,  
5 further comprising the steps of diagnosing an abnormality or disease based on said determining step and treating said abnormality or disease.

24. A method for detecting a pathological condition according to Claim 1,  
wherein said comparing step detects an additional spectral peak in said response  
10 spectrum not present in said standard spectrum, and wherein said determining step is based on the presence of said additional spectral peak.

25. A method for detecting a pathological condition according to Claim 1,  
wherein said comparing step detects the absence of a peak in said response spectrum  
15 which is present in said standard spectrum, and wherein said determining step is based on the absence of said spectral peak.

26. A method for detecting a pathological condition according to Claim 1,  
wherein said comparing step detects an abnormally-sized spectral peak at a  
20 corresponding frequency shift in said response spectrum compared to said standard spectrum, and wherein said determining step is based on the magnitude of the abnormally-sized spectral peak.

27. A method for detecting a pathological condition according to Claim 1,  
25 wherein said at least one region of interest is a plurality of regions of interest and wherein said at least one pathological condition is a plurality of pathological conditions.

28. A method for detecting the presence of atherosclerosis in the coronary  
30 arteries, comprising:

administering a bolus of hyperpolarized  $^{129}\text{Xe}$  gas *in vivo* to a patient so that said hyperpolarized  $^{129}\text{Xe}$  travels to a region of interest;

applying at least one resonant RF pulse sequence to said hyperpolarized  $^{129}\text{Xe}$  in the region of interest;

acquiring at least one response signal spectrum representing the response of said hyperpolarized  $^{129}\text{Xe}$  to said at least one pulse sequence via magnetic resonance spectroscopy;

identifying at least one spectral peak of interest in said response signal spectrum;

analyzing said at least one spectral peak of interest in said response signal spectrum; and

determining the presence of atherosclerotic plaques on the basis of said analyzing and identifying steps.

29. A method for detecting atherosclerosis according to Claim 28, wherein said at least one response signal spectrum comprises a first background signal spectrum and at least one additional signal spectrum of said hyperpolarized  $^{129}\text{Xe}$  in said patient's heart, and wherein said analyzing step comprises the step of subtracting said background signal spectrum from said at least one additional signal spectrum to produce at least one corrected signal spectrum.

30. A method for detecting atherosclerosis according to Claim 29, wherein said acquiring step is carried out subsequent to said administering step such that at least a predetermined threshold amount of  $^{129}\text{Xe}$  is present in said patient's heart.

31. A method for detecting atherosclerosis according to Claim 30, wherein said acquiring step is carried out responsive to a cardiac event.

32. A method for detecting atherosclerosis according to Claim 31, wherein said step of acquiring said background spectrum is cardiac-gated by the same cardiac event but performed prior to said step of acquiring said at least one additional spectrum.

33. A method for detecting atherosclerosis according to Claim 28, wherein said at least one signal spectrum is a plurality of signal spectra.

34. A method for detecting atherosclerosis according to Claim 31, wherein  
5 said at least one resonant RF pulse sequence is selected to produce small flip angles in said hyperpolarized  $^{129}\text{Xe}$ .

35. A method for detecting atherosclerosis according to Claim 28, further comprising normalizing said at least one spectral peak of interest in said corrected  
10 spectrum.

36. A method for detecting atherosclerosis according to Claim 28, wherein said analyzing step further comprises (a) determining at least one selected parameter of said at least one spectra of interest, said selected parameter including at least one of  
15 the amplitude, the area under the curve, the width, and the line shape of said at least one spectral peak of interest in said at least one corrected spectrum and (b) comparing said selected parameter to a corresponding selected peak parameter in a reference standard spectrum.

37. A method for detecting atherosclerosis according to Claim 36, wherein  
20 said selected parameter is the size of said at least one peak of interest measured by the area under the curve of the spectral peak.

38. A method for detecting atherosclerosis according to Claim 28, wherein  
25 said at least one spectral peak of interest is normalized by taking the ratio of a value associated with the spectral peak of interest to the value of a spectral peak associated with plasma-dissolved  $^{129}\text{Xe}$ .

39. A method for detecting atherosclerosis according to Claim 28, wherein  
30 said at least one spectral peak of interest is normalized by taking the ratio of a value associated with the spectral peak of interest to the value of a spectral peak associated

with dissolved phase  $^{129}\text{Xe}$  in the red blood cells, wherein the value is one of the area under the curve or the amplitude of the spectral peaks.

40. A method for detecting atherosclerosis according to Claim 28, wherein  
5 at least one of said resonant RF pulse sequences produces small flip angles in said hyperpolarized  $^{129}\text{Xe}$ .

41. A method for detecting atherosclerosis according to Claim 40, further comprising the steps of:  
10 detecting the signal level of said hyperpolarized  $^{129}\text{Xe}$  in said region of interest; and

changing said RF pulse sequence to increase the associated flip angles of the  $^{129}\text{Xe}$ , wherein said changing step is performed responsive to when the level of hyperpolarized  $^{129}\text{Xe}$  reaches a predetermined level in said region of interest.

15

42. A method for detecting atherosclerosis according to Claim 28, wherein said region of interest is at least one carotid artery.

43. A method for detecting atherosclerosis according to Claim 42, wherein  
20 said at least one RF pulse produces a large flip angle.

44. A method for detecting atherosclerosis according to Claim 28, wherein said RF pulse is delivered to obtain a spectrum based on at least one contrast parameter chosen from the group consisting of D,  $T_1$ ,  $T_{1\rho}$ ,  $T_2$ , and  $T_2^*$ .

25

45. A method for detecting atherosclerosis according to Claim 28, wherein said RF pulse sequence is a  $T_2$ -weighted pulse sequence selected to filter out hyperpolarized  $^{129}\text{Xe}$  signal associated with the blood cells and plasma in the region of interest.

30

46. A method for detecting atherosclerosis according to Claim 28, wherein said RF pulse sequence is a  $T_1$  based pulse sequence selected to filter out



hyperpolarized  $^{129}\text{Xe}$  signal associated with the blood cells and plasma in the region of interest by delaying the signal acquisition a predetermined time after administration of the hyperpolarized gas to the patient, the predetermined time being about 10 seconds to 1 minute after cessation of the *in vivo* administration.

5

47. A method for detecting a pathological condition according to Claim 28, wherein said administering step is carried out by breath-hold delivery during which the patient inhales a quantity of hyperpolarized  $^{129}\text{Xe}$ , holds his or her breath, and then, after a suitable time, exhales to resume normal breathing, and wherein said  
10 RF pulse sequence is initiated after said patient exhales.

48. A method for detecting a pathological condition according to Claim 28, wherein the region of interest comprises at least one of the carotid arteries.